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LETTERS TO THE EDITOR

A cutaneous cyst caused by brucellosis with a negative serological test

We report the case of a male patient with a cutaneous cyst caused by Brucella with a negative serological test, which was successfully treated with doxycycline and rifampin.

A 45 year-old male patient (a farmer) was admitted to our department because of daily febrile spikes of 38 °C, night sweating and arthralgia. The symptoms had started 10 days previously. He had a negative past medical history with no respiratory problems.

On clinical examination, his general condition was satisfactory apart from a rectal temperature of 37.5 °C. A cyst with dimensions of 18 × 12 cm had appeared in the right lumbar area, which was mobile and not painful (Figure 1). It had developed two months earlier and was increasing steadily in size.

A complete blood count and blood chemical tests were within normal limits. X-rays of the chest and thoracic vertebrae did not elicit any pathology; this was also the case with an abdominal ultrasound. The immunoprofile including rheumatoid agglutinin, complement levels (C3, C4), Mantoux test, serum antibody titer for brucellosis, and rose Bengal test were all within normal limits. Antibodies to HIV, Epstein—Barr virus, toxoplasma and cytomegalovirus were also negative. Blood cultures were sterile.

Figure 1 A cyst of 18 × 12 cm dimension, which was mobile and not painful, appeared in the right lumbar area.

After a week of hospitalization, a diagnosis was obtained from the cytological examination of the cystic fluid. Thirty milliliters of thick material was aspirated and sent to the laboratory for routine culture. The fluid had lymphocytosis with low glucose levels and a positive titer for brucellosis 1/640 by the microagglutination test. Fluid cultures yielded growth of a non-motile, Gram-negative, catalase- and oxidase-positive coccobacillus.

The patient was treated with doxycycline (100 mg twice daily) and rifampin (600 mg daily) for six weeks with clinical improvement and gradual disappearance of the cyst during a 1-year follow-up.

Brucellosis is a prevalent bacterial zoonosis.[1] Skin complications are infrequent and affect less than 6% of patients.[2,3] Other authors have found incidence varying from 2% to 11%.[4] The various skin manifestations described in the literature include non-pruritic purpuric lesions from leukocytoclastic vasculitis, urticaria-like papules and plaques, papulonodular eruption and tiny papules on the trunk and proximal extremities, multiple mucocutaneous abscesses, or erythema nodosum-like deep dermal nodules on the legs.[3,5—9] Brucella agglutinin test results have been persistently negative.[5,9]

To our knowledge, there have been few reported cases of soft tissue abscesses not originating from a leak with an internal focus (such as thoracic spondylitis), caused by Brucella with a negative serological test.[4]

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Hyponatraemia associated with lopinavir–ritonavir?

Hyponatraemia is an unusual complication of treatment with highly active antiretroviral therapy (HAART) and to our knowledge has not been reported in association with the use of lopinavir–ritonavir in adults.[1] Common to the protease inhibitor class of antiretrovirals, the important well-recognized side effects of lopinavir–ritonavir include hepatic dysfunction, diabetes, and lipodystrophy syndrome with an increased risk of pancreatitis.[2]

A 42-year old Zimbabwean man presented in July 2005 with confusion, headaches, blurring of vision, myalgia, dysphagia, and weight loss. He was noted to have oesophagopharyngeal candidiasis, bilateral uveitis, and was confused with an expressive dysphasia. HIV serology was positive with a CD4 count of 30 cells/μL and HIV viral load of 380 847 copies/mL. MRI of the head demonstrated symmetrical white matter changes throughout the hemispheres in keeping with an HIV dementia. CSF sampling showed 10 lymphocytes, 0 polymorphs, no organisms on Gram stain, glucose 4.5 mmol/L (serum 8.9 mmol/L), and protein 0.69 g/L. CSF PCR for herpes simplex virus, varicella-zoster virus, enterovirus, mycobacteria, and JC virus was negative as was cryptococcal antigen and mycobacterial culture. Toxoplasma and syphilis serology was negative and cytomegalovirus viral load in blood was <50 copies/mL. An EEG was normal. He was treated with fluconazole 200 mg once daily, co-trimoxazole 960 mg three times per week, and topical cyclopentolate (1%), dexamethasone (0.1%), and timolol (0.25%) for uveitis. Subsequently he was commenced on HAART with lamivudine 150 mg twice daily, tenofovir 245 mg once daily and lopinavir–ritonavir three tablets twice daily. Blood biochemistry demonstrated a mild hepatitis with a transient rise in ALT to 184 IU/L prior to the introduction of HAART and probably secondary to fluconazole. After five days of HAART he was discharged with a declining ALT and plasma sodium of 133 mmol/L having been within the normal range (135–145 mmol/L) on admission.

Two days later he was readmitted with worsening confusion. He was clinically euvolemic and had a Glasgow coma score (GCS) of 14/15. Investigations showed that cranial imaging was unchanged but there was marked derangement in electrolytes with a serum sodium of 111 mmol/L, potassium 4.8 mmol/L, urea 5.4 mmol/L, and creatinine 80 mmol/L. Urine analysis was negative for protein, blood, nitrites, and leukocytes. During the first five days of admission, the paired urine and plasma osmolality ranged between 330 and 732 mOsm/kg and between 239 and 255 mOsm/kg, respectively. The patient had a raised urine sodium of 76 mmol/L. The low plasma osmolality, raised urine osmolality, and raised urine sodium indicated a syndrome of inappropriate secretion of antidiuretic hormone (SIADH). Repeat CSF sampling was acellular, glucose 2.3 mmol/L (serum glucose 4.9 mmol/L), and protein 0.34 mmol/L. He was treated for SIADH by fluid restriction and HAART was discontinued since temporally this was the most likely cause. Investigations to identify an alternative etiology were negative including thyroid function, synacthen test (serum cortisol response to intramuscular tetracosactide) for adrenal insufficiency, chest X-ray, and a septic screen. EEG demonstrated intermittent bursts of a partial seizure pattern. Anticonvulsant therapy with sodium valproate was commenced. Over six days the serum sodium returned to normal. HAART was reintroduced with lamivudine 150 mg twice daily, tenofovir 245 mg once daily, and atazanavir–ritonavir. Electrolytes remained normal and subsequently tenofovir was substituted with abacavir, since the latter has greater CNS penetration and may be beneficial in the setting of HIV dementia.[3,4]

Use of lopinavir–ritonavir is set to rise as clinical trials suggest superior clinical efficacy, no known de novo resistance in treatment-naïve individuals, and a reported side-effect profile to date that is favorable.[5,6] Since the only change in the second HAART regimen was a switch from lopinavir to atazanavir, this report indicates that lopinavir was the most likely cause of the abrupt drop in sodium when using lopinavir boosted with ritonavir. Normal urine analysis did not suggest any direct tubular damage. Drugs used in the management of HIV-related infections are known to precipitate hyponatraemia through an SIADH effect (pyrazinamide, ethambutol),[7] an amiloride-like effect on the renal tubules (high dose trimethoprim),[8] or by as yet undefined mechanisms (amphotericin B, pentamidine).[8] HAART-associated hyponatremia is rare and described only with zalcitabine (Roche® product information) and lopinavir–ritonavir in children.[1] Laboratory investigations indicate that induction